

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference X14441	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2004/009283	International filing date ( <i>day/month/year</i> ) 14 April 2004 (14.04.2004)	Priority date ( <i>day/month/year</i> ) 18 April 2003 (18.04.2003) ]
International Patent Classification (IPC) or national classification and IPC C07D 211/44, 211/54, 401/12, 409/12, A61K 31/445, A61P 25/06		
Applicant ELI LILLY AND COMPANY		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Box No. I   | Basis of the report   |
| <input checked="" type="checkbox"/> Box No. II  | Priority  |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/> Box No. IV             | Lack of unity of invention  |
| <input checked="" type="checkbox"/> Box No. V   | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI             | Certain documents cited   |
| <input type="checkbox"/> Box No. VII            | Certain defects in the international application  |
| <input type="checkbox"/> Box No. VIII           | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Date of issuance of this report 21 October 2005 (21.10.2005)
	Authorized officer  Simin Baharlou Telephone No. +41 22 338 71 30

Form PCT/IB/373 (January 2004)

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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 04 AUG 2004

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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2004/009283

International filing date (day/month/year)  
14.04.2004

Priority date (day/month/year)  
18.04.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D211/44, C07D211/54, C07D401/12, C07D409/12, A61K31/445, A61P25/06

Applicant  
ELI LILLY AND COMPANY

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/009283

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/009283

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**Box No. II    Priority**

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1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/009283

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 10-15

because:

☒ the said international application, or the said claims Nos. 10-15 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 10-15

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/009283

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**Box No. V Reasoned statement under Rule 43b/s.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-28
	No: Claims	
Inventive step (IS)	Yes: Claims	1-28
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-9, 16-28
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

(III)

Claims 10-15 are directed to a method of treatment of the human/animal body and therefore no preliminary examination is required (Rule 67.1(iv) PCT).

Moreover, it is noted by the IPEA that for the assessment of Claims 10-15 on the question whether their subject-matter is industrially applicable, no unified criteria exist in the PCT. The patentability under national patent laws can also be dependent on the formulation of the claims. The EPO, e.g., does not recognize the subject-matter of claims to the use of a compound in medical treatment as being industrially applicable, but will allow, however, claims to a known compound for the manufacture of a medicament for a new medical treatment.

(V)

Having regard to the International Search Report as well as the prior art cited by the Applicant in the description the claimed subject-matter differs from document (D1) WO 00/47599 due to the present definition of "A, R<sup>1</sup>" therein compared with present -N-R<sup>3</sup>-C(=O)R<sup>1</sup> and R<sup>4c</sup> respectively.

Moreover, it is noted by the IPEA that doc.(D2) WO 03/084949, a P-document not relevant at this stage, discloses similar compounds bearing a carbonyl link group, thus differing from present "Q" group.

It is further noted that the reasons for introducing the disclaimer with regard to R<sup>5</sup>/R<sup>6</sup> into Claim 1 are not clear with regard to the structural difference vis a vis (D1), or even (D2).

The requirements of Art.33(2) PCT appear to be fulfilled.

The problem underlying the present invention appears to be the provision of further compounds useful as 5-HT<sub>1F</sub>-anti migraine agents. The novel structural features of the present compounds, when compared with the anti-migraine compounds known from (D1) or the common technical knowledge, are not considered to be derivable in an obvious manner. The solution to the technical problem thus appears to be non obvious in the light of (D1).

Accordingly the requirements of Art.33(3) PCT appear to be fulfilled, provided that all compounds claimed under formula (I) possess the desired 5HT<sub>1F</sub>-agonistic properties. In this respect reference is made to the fact that no compounds appear to have been prepared and tested by the Applicant wherein R<sup>2</sup> is other than methyl; R<sup>1</sup>= (substituted) heterocycle does not specify the number of carbon- or heteroatoms, thus appearing to be vague and speculative in this respect.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/009283

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